STUDY OF 70 CASES OF POSTERIOR UVEITIS TO EVALUATE THE VARIOUS ETIOLOGIES AND MANAGEMENT

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CERTIFICATE

This is to certify that this dissertation titled **" STUDY OF 70 CASES OF POSTERIOR UVEITIS TO EVALUATE THE VARIOUS ETIOLOGIES AND MANAGEMENT"** is a bonafide work done by **Dr.ASHISH AMAR,** M.S. Post Graduate Student of Ophthalmology Regional Institute of Ophthalmology, Govt. Ophthalmic Hospital, Egmore, Chennai - 600 008 attached to Madras Medical College, during the academic year 2003-2006.

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PART I

INTRODUCTION

- Uveitis refers to inflammation of the middle vascular tunic of the Eye called uvea.

- The name uvea is derived from the Latin word "uva" or grape, consists of three parts the iris, the ciliary body and the choroid.

- Uveitis is extremely important epidemiologically in underdeveloped, developing & developed societies alike accounting for a very large medical & economic burden on population.

- Despite the progress made since the introduction of steroid therapy in 1950; large number of patients eventually are blinded by the consequences of recurrent or chronic uveitis; this problem is consistently agreed to be the 3rd leading cause of preventable blindness in all developed societies.

- If we ever hope to reduce the prevalence of blindness that is secondary to uveitis, ophthalmologists in large numbers must embrace a philosophy of earlier; more aggressive therapy with a limit to the total amount of steroid ultimately used.

HISTORICAL REVIEW

1500 - Eben's Pappyrus mentioned about congestion of Eyeball

1722 - Charles Saint Yyes described about clinical symptoms like Redness, Lacrimation, photophobia, and pain.

1801 - Johann Adam introduced the term Iritis.

1829 - Fredrich Vonammon - inflammation of orbicularis ciliaris

1853 - Von Arlt - gave causes of uveitis - Scrofula 30%, Rheumatism 25%, Syphilis 17% & Idiopathic 25.5%

1866 - Von Graefe & Ernest Fuch's described cyclitis.

1869 - Hutchinson initially described sarcordosis as skin disease.

1881 - Von Michael emphasized the importance of Tuberculosis as cause of uveitis.

1892 - Nettleship considered a case of Exudative choroiditis due to dental infection.

1908 - Toxoplsma Gondii isolated from North African Rodent by Nicollex Manceaux

1931 - Kolmer puts forward role of bacterial toxin & allergy as uveitis cause.

1940 - Brucellosis and Sarcoidosis were recognized as clinical entities.

1946 - Allan `C' wood considered that 79% of Granulomatous uveitis was due to Tuberculosis.

1950 - Toxoplasmic uveitis became a proven infection & thus parasitic infection played a considerable role in the etiology of posterior uveitis

1960 - Alan Churchill Woods described in detail about Endogenous uveitis.

1961 - Woods considered Histoplasmosis to be cause of 13% of uveitis.

1990 - The effect of uveitogenic antigens on the eye & the immune response peculiar to the ocular structure have become the major subject of research.

CLASSIFICATION OF UVEITIS

A) Anatomical Classification by International Uveitis Study Group (IUSG)

1. Anterior

- Iritis
- Anterior cyclitis
- Iridocyclitis

2. Intermediate

- Posterior Cyclitis
- Hyalitis
- Basal Retinochoroiditis

3. Posterior

- Chorioretinitis
- Retinochoroiditis
- Neurouveitis
- Choroiditis
    - Focal
    - Multifocal
    - Diffuse.

4. Panuveitis

B) Etiological Classification

Group 1: Idiopathic

1a: With only ocular features

1b: With both ocular and systemic features

Group 2: Infections

2a: With only Ocular features

2b: With both ocular and systemic features

Group 3: Non-infections

3a: With only ocular features

3b: With both ocular & systemic features

C) Clinical Classification

On duration and onset

- ♣ Acute
- ♣ Chronic
- ♣ Recurrent

On Activity

- ♣ Active
- ♣ Resolved

On Clinical Features

- ♣ Granulomatous
- ♣ Non Granulomatous

On complications

- ♣ Simple
- ♣ Complicated

On threat to Vision

- ♣ Mild
- ♣ Severe

ANATOMY OF UVEA

The uvea consists of the iris, ciliary body and choroid. Iris forms a diaphragm perforated by the pupil, the peripheral root of the iris arises from the anterior end of the ciliary body, which is attached to the sclera 2mm behind the limbus.

IRIS

The anterior surface of the iris is divided into an inner 1-2mm wide pupillary zone and outer ring called ciliary zone. At the junction of pupillary and ciliary zone is a frill called collarette. The anterior surface of the iris bears numerous radial furrows, while the posterior surface bears concentric furrows of schwalbe.

LAYERS OF THE IRIS

1) **Anterior Endothelium**: Present only as island at places.

2) **Anterior Limiting Border layer**: is the anterior condensed part of stroma, which contains blood vessels, nerve endings & pigment cells.

3) **Stroma:** Major & Minor arterial circles are situated here. The smooth muscle sphincter pupillae is present which is supplied by short ciliary nerves.

4) **Posterior Membrane:** Layer of smooth muscle fiber called dilator pupillae.

5) **Posterior Epithelium**: This consists of two layers of richly pigmented cells.

CILIARY BODY

It extends for 6mm from the root of Iris to the ora serrata. The posterior two thirds, the pars plana has a smooth black surface, marked only by faint striae- ciliaris, running on the teeth of the ora serrata while the anterior third - parsplicata bears about 72 radial ridges, or ciliary processes. It is from these the fibres of Zonules take origin.

NERVE SUPPLY: The main supply is via short ciliary nerve.

BLOOD SUPPLY: Long Posterior & Anterior Ciliary arteries

CHOROID

It is the most posterior part of vascular coat of Eye. It is thin, soft, brown coat lining the inner surface of the sclera. It is extremely vascular. It is thickest at the posterior pole (about 0.22mm) & gradually thins anteriorly (about 0.1mm). Its inner surface is smooth & firmly attached to the pigmented layer of the retina; its outer surface is roughened. It is firmly attached to the sclera in the region of the optic nerve and where the posterior ciliary arteries and ciliary nerves enter the Eye. It is also tethered to the sclera where the vortex veins leave the Eyeball. At the optic nerve the choroid becomes continuous with the pia and arachnoid.

LAYERS OF THE CHOROID

1. **Suprachoroid lamina of Fusca:** This is the layer of choroid in relation to sclera. It is 10-34μ in thickness. It contains a delicate meshwork of Elastin fibres. These are lined by endothelium and enclose potential lymphatic spaces. The spaces become evident, when pathologically distended with fluid, giving an appearance of a grill. The layer contains fibrocytes (called chromatophores) with short processes and pigment. Pigments are more in the posterior aspect. This layer consists the long and short ciliary nerves and vessels.

2. Layers of Haller and Sattler: These are the layers of blood vessels. The layer of Haller contains large vessels whereas in the layer of Sattler vessels are medium sized. The stroma in these layers contains collagen and elastic fibres. Stellate pigment cells or chomatophores are present. The size of pigment granules in them is same in one individual but differs from race to race. The choroid pigments prevent the passage of light through the sclera. They absorb the light traversing the retina, preventing internal reflection within vitreous body.

3. Layer of Choriocapillaries: The capillaries in this layer are of wide bore. Pigment cells are absent. The choroicapillaries end in the ora serrata, whereas the outer layers continue to the ciliary body. The capillaries form dense network at the macula and also show sac like dilatations. The choriocapillaries supply the outer part of the retina.

4. Membrane of Bruch (Basal Lamina of Bruch): This is a structure less glossy, homogenous membrane about 1.5μ in thickness and is also called lamina vitrea. This layer consists of two sheaths. The function of this membrane is not well defined. Probably it helps in the passage of nutrients to retina and provides a smooth surface for the precise orientation of the RPE and receptors.

NERVE SUPPLY: The vessels of the suprachoroid and stroma show a striking dense parasympathetic and sympathetic innervations. Sympathetic Adrenergic fibers, which arise from cervical sympathetic chain, have a vasoconstrictor action. The parasympathetic innervations of the choroid are from the facial nerve and pterygopalatine ganglion and from oculomotor nerve via ciliary ganglion and short ciliary nerves. They serve as vasodilator role perhaps adjusting blood flow in response to reduction in arterial blood pressure or protecting the retina from thermal damage associated with light exposure.

BLOOD SUPPLY: The short posterior ciliary arteries supply the posterior choroid upto the equator and a variable area anterior to it. The temporal long posterior ciliary artery supplies a wedge shaped sector of the choroid starting from point it enters the choroid posterior to the equator and extending forwards. The anterior part of the choroid is otherwise supplied by recurrent ciliary arteries, which arise in the ciliary body from circulus iridis major and from the long posterior and anterior ciliary arteries before they join the muscular circle.

ANATOMICAL AND FUNCTIONAL VASCULAR UNITS OF THE CHOROID

Hayreh (1974, 1975, 1990) and Torazynstri & Tso (1976) showed in human studies that each terminal arteriole appeared to supply an independent segment or lobule of choriocapillaries compromising a central feeding arteriole, capillary bed and a series of peripheral draining venules.

CHOROIDAL ANATOMY & CIRCULATION IN RELEVANCE TO CHOROIDITIS

The choroid has a blood flow that is comparable only to the kidney. Therefore systemic influences can be assumed to rapidly affect this portion of the eye. Indeed the relative large blood flow and its anatomy would act as a sort of trap for many blood borne problems most notably fungal disorders. Therefore most fungal lesions begin as choroiditis. The choroid has a capacity to function as a repository for immunoreactive cells in the extreme stages, taking on the anatomic structure of a lymph node (lymphoid hyperplasia). Therefore this organ can be center for profound immune responses. The high concentration of mast cells in the choroid may be one of the mechanism by which immuno reactive cells in the choroid could spread to other parts of the eye.

UVEITIS PATHOGENESIS AND RELATED IMMUNOLOGY

One of the oldest & major hypothesis is the concept of direct bacterial invasion. Another hypothesis for recurrent ocular inflammation assumes a structural alteration within the eye resulting from a previous inflammation that predisposes the eye to recurrent inflammatory episodes. Some acknowledged facts in pathogenesis are:

FOCAL INFECTION: Any focal sepsis is a predisposing factor for uveitis since most of the ocular inflammation is infective in nature. Among the foci of infection the teeth is considered the most prolific source. The others being the tonsils, para nasal sinuses, respiratory tract, skin, alimentary tract, uterus and the urinary tract.

PROSTAGLANDINS AS AETIOLOGIC UNIT: Prostaglandin is a chemical mediator involved in the pathogenesis of uveitis. Prostaglandin causes dramatic increase in protein content in aqueous humor and vitreous.

VITREOUS ANTIGEN DEPOT: Once Antigen gains access to the vitreous body, it tends to persist. One reason for this is that hyaluronic acids form stable complexes with antigens. This depot type of situation tends to enhance and prolong immune response to trapped antigen. Since Hyalocytes have macrophagic character, they may promote a persistent tendency to recurrence of uveitis by processing antigen and modulating the immune responses.

UVEA AS A NODE: When the antigen is introduced at a distance site or is injected directly into the circulation, antibody production begins inside the eye.

The specific antibody produced takes up residence within the uvea and remains there for long period. Here the new antigen is needed to stimulate them for the renewal of the antibody response.

IMMEDIATE HYPERSENSITIVITY (ANAPHYLAXIS): This results from contact of the uveal tissue to some foreign protein namely bacterial protein, where an immediate antigen Antibody reaction occurs.

DELAYED HYPERSENSITIVITY (BACTERIAL ALLERGY): The tissues are sensitized by contact with living or dead organism so that further contact with same antigen causes severe cellular damage, which develops slowly causing an inflammatory, and necrotic tissue reaction.

IMMUNE CHARACTERISTICS OF THE EYE: For years the Eye was considered to be a "Privileged Immune Site" - implication of this term was that the immune system somehow ignored or was tolerant of the antigens in the Eye. As with Brain, placenta, testes, Eyes have no direct lymphatic drainage although in mice submandibular nodes do collect antigen from the eye.

FOUR MECHANISMS BY WHICH EYE PROTECTS ITSELF FROM UNWANTED NUISANCES

1. Blood ocular Barrier
2. Presence of soluble/membrane bound inhibitors that block function of an organism.
3. Kill an invading organism / cell that may be inducing an unwanted inflammation (by speeding up Apoptosis)
4. Tolerance is induced inside the eye.

IMMUNE RESPONSE TO INVADING VIRUSES & PARASITES

- Certain viruses have a particular propensity for retinal tissue with Herpes family infections particularly CMV being of ever increasing concern.

- Cellular immune mechanism appears to play a crucial role in eliminating the invading virus. Any damage to this system could lead to grave consequences. This is the case with infection due to HIV: have secondary repercussions in the body's attempt to clear other viral infections such as CMV.

- The classical described response to parasitic infections is an eosinophilia. The release of basic protein and other toxic produces from the eosinophil is thought to kill the organism. Eosinophilia is characteristic for some forms of ocular parasitic infections such as toxocariasis. However for other infections such as toxoplasmosis and onchocerciasis, T cells seen to predominate in the Eye & deficient T cell functioning lead to serious consequences --> systemic and ocular toxoplasmic infection seen in patients with AIDS.

- Immunosuppressive factors appear to be elaborated by the parasite leading to a downgrading of macrophage & T cell activity around it.

- Certain parasites cloak themselves in non-antigenic proteins avoiding immune attack eg. toxoplasma cyst.

CLINICAL FEATURES OF POSTERIOR UVEITIS

SYMPTOMS

A careful and detailed medical history is one of the keys to correct diagnosis in the patient with uveitis. Floaters and decreased vision are the two most common complaints of patients with inflammation of the vitreous, retina and choroid. Most patients describe floaters as multiple small or medium sized spots that moves as their eye moves. Other patients complain of blurred or decreased vision. Infact, when visual acuity is severely diminished, patients may be unable to visualize the floaters and these patients may only complain of floaters as vision starts to improve after therapy. A change in the pattern of floaters or visual impairment often signals a change in the underlying ocular disease. A patient with a peripheral inflammatory lesion will complain of floaters and may have only minimal blurring of vision. On the other hand, active choroiditis involving fovea will usually cause loss of central vision.

SIGNS

The ocular examination of patients with uveitis is important not only to diagnose the disease appropriately but also to determine the appropriate therapy.

SLIT LAMP BIOMICROSCOPY

1. **Ciliary Injection**: results from engorgement of the radial episcleral vessels and is seen as violaceous hue around the limbus.

2. **Keratic Precipiatates:** They are small aggregates of inflammatory cells that accumulate on the endothelial surface of the cornea.

3. **Flare:** this is turbidity of the ocular media (aqueous/vitreous) due to transudation of proteins across the inflamed blood vessels. It is a sign of disruption of the blood ocular barrier.

Grading of Anterior Chamber Flare by Hogan et al.

Flare Grade	Description
0	Complete Absence
1+	Very Slight (Faint Flare)
2+	Iris & Lens details clear (Moderate Flare)
3+	Iris & Lens details hazy (Marked Flare)
4+	Fixed Coagulated aqueous with considerable fibrin (Intense Flare)

4. **Cells:** Depending on the nature and severity of inflammation, various cells may migrate across the iris and ciliary vasculature into the aqueous and vitreous. The vitreous is rarely a source of inflammatory cells except in certain situations.

Grading of Anterior Chamber Cells by Nussenblatt et. al.

Grade	No. Of Cells
0	0
1+	< 10 Cells
2+	11-20 Cells
3+	21-50 Cells
4+	> 50 Cells
Hypopyon	

5. **Grading of Vitreous Haze:** Vitreous haze is a better indicator of active inflammation than vitreous cells because it combines the optical effect of cellular infiltration and protein leakage. Grading scale is based on the view of the optic disc and posterior retina with the use of the indirect ophthalmoscope and a 20D lens. It is important to mentally correct for lens opacities, anterior segment inflammation and corneal disease. The use of photographic standards makes this system more reproducible.

Grade	Description
0	Nerve Fiber Striations well defined
1+	Better definition of optic Nerve Head and Retinal blood vessels
2+	Better visualization of retinal blood vessels
3+	Optic Nerve Head Visible but its borders blurred
4+	Optic Nerve Head obscured

6. **Grading of Vitreous Cells:** The vitreous is larger cells may be localized to only a part of vitreous. Therefore the quantification may depend on how the eye is examined. The Grading of vitreous cells described by **Kimura & Colleagues** uses the Hruby lens to view the cells in retro illumination. The cells appear as black dots.

Grade	Cells in Retroilluminated Field	Description
0+	0-1	Clear
Trace	2-20	Few Opacities
1+	21-50	Scattered Opacities
2+	51-100	Moderate Opacities
3+	101-250	Many Opacities
4+	>251	Dense Opacities

The cells appear as black dots and it may be difficult to differentiate uveal debris from active inflammatory cells. Debris is often pigmented and form clumps that are longer than individual cells.

7. Retina & Choroid

Examination is best done with a combination of indirect ophthalmoscope, Hruby lens, +90D lens and a mirrored contact lens.

i) Cystoid Macular Edema: is a common retinal finding in patients with uveitis. Although Fluorescein angiography can more definitively document the presence of macular edema, clinical examination with the Hruby lens is easier, cost effective, determines the extend of macular thickening associated with Edema and can be performed on each visit. In the presence of vitreous haze it is best observed by viewing with light directed slightly to one side of the fovea.

ii) Retinal Vascular alterations: Vascular sheathing of arteries (periarteritis) and veins (periphlebitis) by infiltration of inflammatory cells around the vessels is easily seen in posterior pole. Periphlebitis is commoner than periarteritis, both being characterized by fluffy white haziness surrounding the blood column. Vessel narrowing, obliteration, retinal hemorrhages and cotton woolspots often accompany. Peripheral vascular sheathing and narrowing is subtler and is best evaluated with the indirect ophthalmoscope.

iii) Choroidal Lesions: When deep or isolated to choroid appear as grayish - yellow demarcated masses. One or more choroidal nodules may be

present and can vary in size from 50 μm to 500 μm in diameter. Atrophic chorioretinal lesions with surrounding hyper pigmentation are a striking sign of inflammatory disease in the patients with uveitis. Although the appearance of inflammatory lesions of the retina and choroid can vary greatly, some lesions have a characteristic presentation and can help in diagnosis. Eg. Dalen Fuchs nodules tend to be small, discrete, deep, yellow white lesions that may be associated with hyperpigmentation.

8. Optic Nerve

Uveitis may affect the optic nerve in several ways. Disc hyperemia, papillitis or papilledema may be seen. So, in determining the cause of visual loss in eyes, optic nerve head should not be overlooked. Prominent disc hyperemia is frequently noted in VKH syndrome. Neovascularisation, glaucomatous damage or optic Atrophy may develop in the optic disc. Inflammatory disease like sarcoidosis may directly involve the nerve.

INVESTIGATIONS

Royal College Guidelines: Ordering large number of tests in the hope that one may turn out to be positive should be actively discouraged. Also if one does many investigations on a single patient, there is the chance that something will turn out to be abnormal but it may not have relevance to the etiology of uveitis.

Reasons to Investigate Posterior Uveitis are

1) Come to a specific diagnosis.
2) Confirm a clinical diagnosis.
3) Commence antimetabolite / Immuno suppressive therapy.
4) Identify complications.
5) To explain cause of poor vision
6) Rule out Masquerade Syndromes/infections

1) Haematological Investigations : Estimation of Hb., TLC, DLC, ESR or routine urine analysis are nonspecific and of no help in the diagnosis, hence are not advocated. However, they are important when the patient is to be started on anti metabolites. In these patients, baseline and repeated values are necessary in detecting bone marrow depression and dose adjustment. An important hematological investigation is estimation of CD4/CD8 lymphocyte ratio in patients with suspected HIV infection. In patients with AIDS this is the single best predictor of imminent opportunistic infection. The normal ratio is usually 2.0 and in AIDS patient becomes reversed with value of 0.5 - 1.0.

Hematological Investigations - When?

- Commencing antimetabolite/Immunosuppressive therapy.
- Suspicion of Parasitic Infestation
- Suspicion of Leukemia

2) Immunological Investigation(s)

Some important serological investigations are:

a) Rheumatoid Factor: This is detected by immuno turbimetry and has no role in the diagnosis of uveitic entities. However it forms the basis of dividing arthropathies into seropositive and seronegative.

b) Anti nuclear Antibodies: ANA detection is the most sensitive laboratory test for SLE and is present in 99% of these cases.

c) Anti-DNA Antibodies: Antibodies against double standard DNA are found in 40-80% of cases of SLE and only rarely in other connective tissue disorders.

d) Anti-Neutrophil Cytoplasmic Antibodies (ANCA): ANCA are the group of autoantibodies that occur in a large majority of patients with systemic small vessel vasculitis.

e) Angiotensin Converting Enzyme (ACE): Serum ACE levels are elevated in 85% of patients with active pulmonary disease due to sarcoidosis. S.ACE levels is considered to be elevated if the value is above 35 IU/ml in adults and 50 IU/ml in those below 10 years.

f) Serum Globulin: 75% of patients with sarcoidosis have elevated serum globulin levels.

g) Serum Lyzozyme: In sarcoidosis, serum levels of Lysozyme have been found to be elevated in 70% of cases irrespective of whether the disease is active/inactive.

h) Serological tests for infections agents

i) Toxoplasmosis (IgG)

No previous infection : < 1:16

Prevalent in general population : 1:16 - 1:256

Suggests recent infection : > 1 : 256

Suggests active infection : > 1: 1024

ii) Toxoplasmosis (IgM)

In children : any titer is significant

In adults : > 1:64 indicates active infection.

iii) Herpies Simpler IgM & IgG <1:5 & <1:10 (Negative)

iv) Varicella Zoster (IgG/IgM) <1:10 (Negative)

3) Radiological Investigations

A simple chest X-ray should be done in all cases of uveitis to rule out sarcoidosis. X-ray done at the onset of eye inflammation has greatest likelihood of detecting abnormality as it may become normal despite persistent eye inflammation. It is important to establish the diagnosis of sarcoidosis, since it has prognostic and therapeutic significance.

Radiological Investigations - When?

• Skull	:	Congenital toxoplasmosis
• Chest	:	Sarcoidosis / tuberculosis/malignancy.
• Sacroiliac & Spinal	:	Ankylosing spondylitis
• Gallium Scan	:	Sarcoidosis

Gallium scan may be abnormal in some cases of sarcoidosis. However, its cost, lack of theraupetic implications and non specificity forbids its routine use. Skull X-ray (lateral) to evaluate for calcification in suspected congenital toxoplasmosis case should not be overlooked. Sinus radiography has also traditionally been done in cases of uveitis, however, its value in diagnosis or prognosis is not clear.

4) HLA Typing

HLA antigens are now considered to be the genetic markers for susceptibility. The classical example for this is association of acute anterior uveitis in HLA-B_{27} positive individuals. The other accepted associations are shown below

HLA Typing

• Behcet's disease	:	HLA-B-5
• Birdshot retinochoroidopathy	:	HLA-A29
• Sympathetic Ophthalmia	:	HLA-A11
• Vogt-Koyanagi-Harada Syndrome	:	MT-3/HLA BW 22J

HLA typing is an expensive test and should be ordered only for patients in whom it would make a therapeutic or prognostic difference. It is reserved for patients with an acute onset, anterior, unilateral uveitis. In some cases of Behcet's, the diagnosis may be a problem and confirming it with the HLA typing may help the surgeon to put the patient on immunosuppressives rather than steroids.

5. Skin Test

The basis for all skin tests is delayed hypersensitivity reaction of type IV. Many skin tests are available that can be used for the diagnosis of different etiologies of uveitis. Its main use has been in the diagnosis of tuberculosis and histoplasmosis. Sometimes it has also been used to indicate anergy in cases of sarcoidosis.

Dermatological Tests

• Tuberculosis	:	Mantoux Test
• Histoplasmosis	:	Histoplasmin test
• Sarcoidosis	:	Kveim test
• Anergy	:	Sarcoidosis/leprosy

6) Fluorescein Angiography

It is an important test in evaluating cases of uveitis. FFA is very useful in inflammatory disease due to its ability to visualize retinal vessels and delineate their walls. The inflammation of retinal vessels alters the endothelial tight junctions due to which fluorescein leaks from the vessels. Thus, vasculitis

can be diagnosed well before it is seen clinically. FFA also helps in assessing the leakage of dye from retinal capillaries in the macula and optic nerve in CME & papilliltis respectively; presence of retinal vascular occlusion and retinal and choroidal neovascularisation can be easily seen with FFA. It is helpful in differentiating the active lesion from healed one in retinal and choroidal diseases. In active stage, the margins of the lesion show diffuse staining and blurring. Healed stage shows hyperfluorescence with well-defined margins.

Posterior uveitis entities in which FFA is indicated are

1) Serpiginous choroidopathy or Geographic Helicoid Peripapillary Choroiditis (GHPPC)
2) Sarcoidosis
3) Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE)
4) Multiple Evanescent White Dot Syndrome (MEWDS)
5) Sympathetic Ophthalmia
6) Vogt Koyanagi Harada Syndrome
7) Retinal Vasculitis
8) Bird Shot retinochoroidopathy
9) Behcet's disease
10) Inflammatory Choroidal neovascular membrane (CNVM)

7) Indocyanine Green Angiography (ICG)

The major drawback of FFA is its inability to image the choroid and detect inflammatory conditions affecting the choroid and choriocapilliaries. Flower and Flochheimer introduced this technique, which images the choroid and its associated conditions, in 1970. It uses a tricarbocyanine dye which is 98% protein bound and operates in infrared range. The dye absorbs light at 790 nm and emits at 830 nm. It leaks through fenestrated choriocapillaries thus allowing visualization of choroidal circulation through RPE. Choroidal inflammatory lesions are mostly seen as areas of Hypofluorescence in ICG. Various inflammatory conditions where ICGA is advised are

i) Multifocal choroiditis

ii) APMPPE

iii) MEWDS

iv) GHPPC

v) Birdshot Chorioretinopathy

8) Optical Coherence Tomography (OCT)

It is a relatively newer method of high resolutional cross sectional imaging in retina. It is based on the principle of low coherence interferometry in near infrared range to achieve high resolution of 10-14mm; It directly measure the thickness of retina. In uveitis it is particularly useful in diagnosis and follow up of cystoid macular Edema, macular hole and epiretinal membranes.

9) Polymerase Chain Reaction (PCR)

It has rapidly become established as one of the most widely used techniques of molecular biology. It is rapid, inexpensive and simple means of producing microgram amounts of DNA from minute quantites of source material.

Pathogens Detected by PCR are

CMV, HSV, VZV, EBV, HPV, Hepatitis A,B,C, HIV type I & II, Rubella Rickettsia rickettsii, Borrelia Burgdorferi, Treponema Pallidum Mycobacterium Tuberculosis, Neisseria meningitis, Hemophilis influenza, Streptococci, Staphylococci Toxoplasma Gondii, Pneumocystis Carnii, Acanthamoeba Species.

It is especially useful in Endophthalmitis, atypical toxoplasmosis, viral and tuberculous retinitis.

10) B Scan Ultrasonography

Safe, non-invasive, rapid imaging modality which uses frequencies in the range of 7.5 - 1.5 MHz; for evaluation of posterior globe and orbit. It evaluates the posterior segment in conditions with media opacities such as complicated cataract, vitreous hemorrhage, dense vitritis, corneal opacity, mosed pupil. It is also helpful in diagnosing sympathetic ophthalmia & VKH

syndrome by revealing associated retinochoroidal thickening and exudative retinal detachment.

11) Diagnostic Surgery

AC Paracentesis

Simple and safe procedure, which can be performed by an experienced ophthalmologist. It can be done at the slit lamp or under a microscope in operation theatre. About 0.1-0.3 ml Aqueous fluid is collected with a 27G needle attached to a tuberculin syringe.

Vitreous Tap & Diagnostic Vitrectomy

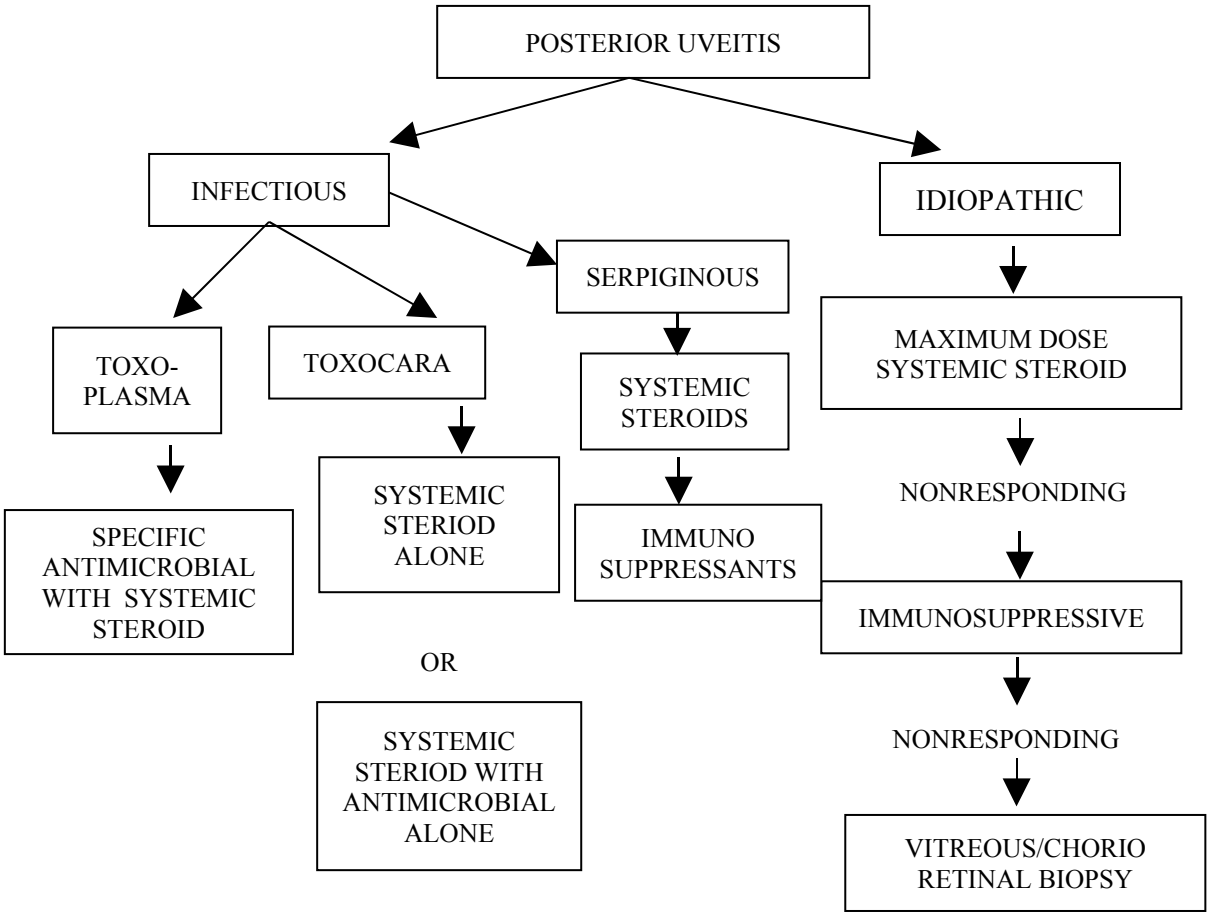
Vitreous fluid analysis is considered in some sight threatening uveitis in diagnostic Dilemmas and Masquerade Syndromes.

Retinal & Chorioretinal Biopsy

In diagnostic dilemmas where inflammation is localised to Retina and RPE tissue biopsy can be performed in order to understand the disease and make a definitive diagnosis. Biopsy site should be at border of active chorioretinal disease and normal retina.

NON SPECIFIC MANAGEMENT IN POSTERIOR UVEITIS

The objective of treatment in a patient is to preserve macular acuity, to preserve visual fields, provide symptomatic relief, to prevent complications and managing any systemic associations if any.



Treatment Protocol in Posterior Uveitis

1) Corticosteroids

The mainstays of anti-inflammatory therapy for most types of uveitis and effectively suppress the inflammatory response regardless of cause. Though these drugs are effective in ameliorating the inflammation in a large majority of patients they have the potential for producing significant ocular and

systemic morbidity. Hence caution is recommended in their use. It is mandatory to elicit specific patient history for diseases such as diabetes mellitus, hypertension, peptic ulceration, osteoporosis etc. that may get aggravated by prescribing systemic corticosteroids. The risk, nature and severity of adverse effects depend both on the dose and duration of treatment.

Cortiosteroids can be administered by 3 routes:

1) Topical
2) Periocular
3) Systemic (oral & parental)

1) Topical costicosteroids

These are absorbed quite well through the cornea and form the mainstay of therapy of anterior uveitis. They do not reach the posterior segment to the desired extend and so have no beneficial effect in posterior uveitis.

2) Periocular Injection

With this modality of treatment maximum concentration in uveal tissue is achieved with minimal systemic side effects. An experimental study has shown that both methyl prednisolone and triamcinolone acetonide penetrate well into the vitreous cavity and retina following posterior sub-Tenon's injection. The effect of short-acting depot steroids lasts for a few hours to one day while the effect of long-acting depot steroids lasts for two to three weeks. A list of the commonly used injectable corticosteroid preparations is given in Table.

COMMONLY USED INJECTABLE CORTICOSTERIOD PREPARATIONS

Short - acting: (Few hours to one day)

Hydrocortisone acetate (25mg/ml)
Btamethasone (4mg/ml)
Dexamethasone (4mg /ml)

Long-acting (2 to 3 weeks)

Methylprednisolone acetate (40 mg/ml)
Triamcinolone acetonide (20 mg/ml) or 40 mg/ml)

Subconjunctival Injection

It is useful in cases of anterior uveitis, which do not respond to topical therapy. Subconjunctival injections are, however, ineffective in posterior uveitis as intraocular penetration is poor.

Posterior sub-Tenon's Injections

Posterior sub-Tenon's injection is recommended in intermediate uveitis and in posterior uveitis along with systemic steroids and in panuveitis along with systemic and topical steroids.

Technique: The best site for injection is the upper temporal quadrant. The upper eyelid is elevated and the patient is instructed to look down and in. One millilitre of the drug is taken in a 2ml syringe with a 27 gauge, 5/8, inch disposable needle. With the bevel towards the globe, the needle is introduced

into the superior bulbar conjunctiva and moved from side to side and injected into the posterior sub-Tenon's space.

Retrobulbar Injection

This is seldom preferred because of the high degree of risk involved in the technique and the poor intraocular penetration of the drug.

Complications related to the effect of depot preparation of periocular corticosteriods include:

- Systemic absorption
- Increased intraocular pressure
- Scarring between conjunctiva and globe
- Posterior subcapsular cataract
- Hypersensitivity tissue reaction
- Subdermal fat atrophy
- Ptosis and extraocular muscle paresis
- Potentiation of infection
- Worsening of infectious uveitis

Systemic Steriods

Systemic steroid therapy is used predominantly in posterior segment involvement. It is also used in cases of anterior or intermediate uveitis, which have not responded to topical therapy.

Oral corticosteroids have several potential hazards. A definite plan of therapy must be made before their use. The common steroid preparations are listed in Table on next page.

Generic Name	Route
Prednisone	Oral
Prednisolone	Oral
Dexamethasone	Oral
Betamethasone	Oral
Methylprednisolone	IM or IV
Cortisone	IV

General guidelines for oral corticosteriod therapy are given below: (Modified from Gordon DM)

- Use enough, soon enough, often enough and long enough to secure the desired results.

- Start with a high dose and taper according to the clinical response. An oral steroid is started with the maximum dosage (1mg/kg of body wt.) and when the desired effect is achieved, is given every alternate day.

- If therapy prolongs for over two weeks, never stop abruptly at a high dosage. Taper it slowly. If therapy is to be discontinued, an attempt should be made to control the disease with periocular injection.

- Suppress inflammation till the pathogenic effect ends. Determine the minimal maintenance dose by a process of trial and error. Make an effort to reduce the dosage if there is no sign of relapse. Increase the dosage immediately in case of recurrence.

- The dosage of steroid should not be tapered with a predetermined plan but in accordance to the response of the disease.

Complications

- Cushingoid features
- Peptic ulceration
- Aseptic necrosis of head of femur
- Osteoporosis
- Steroid - induced diabetes
- Mental changes
- Electrolyte imbalance
- Reactivation of infections
- Cataract
- Increase in the severity of pre-existing disease such as diabetes, hypertension.
- Limitation of growth in children.
- Myopathy

Contraindications

Absolute

- Pregnancy
- Peptic ulcer
- Osteoporosis especially during menopause
- Active infection

Relative

- Diabetes mellitus
- Hypertension
- Cardiovascular disease

Immunosuppressive Agents

Immunosuppressive agents are now the first choice of therapy for corticosteriod - resistant cases of uveitis and in cases where corticosteroids are contraindicated.

The side effects and potential complications of these agents are many and at times fatal. These are therefore reserved as the second line of treatment in many cases, the first being corticosteriods.

An immunosuppressive agent should be used with caution. A generalized guideline for the use of immunosuppressive drugs is given below.

Immunosuppressive agents are used only when:

- Uveitis is vision - threatening
- Reversibility of the disease process is possible.
- An objective evaluation of the process of disease is possible
- No response to an adequate regimen of corticosteriods is found.
- Systemic corticosteriods are contraindicated.
- Active infection is absent
- Hematological contraindication is absent.
- The patient understands the needs for a periodic follow-up by the ophthalmologist and the internist.
- Informed consent is obtained.

In 1980, the International Uveitis Study Group (IUSG) recommended a guideline for the use of immunosuppressive agents, which is given in Table in next page.

GUIDELINE FOR USE OF IMMUNOSUPPRESSIVE AGENTS IN UVEITIC DISEASE

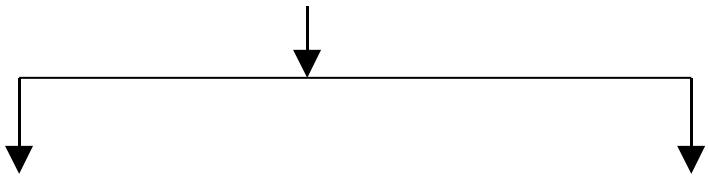
Absolute	:	Behcet's disease, sympathetic ophthalmia.
Relative	:	All cases unresponsive to maximum steroid therapy
Questionable	:	Eales' disease, Retinal vasculitis, serpiginous choroidopathy
Contraindicated	:	Focal chorioretinitis, herpetic disease, toxoplasmosis, cytomegalovirus, and fungal infection.

Immunosuppressive Agents: Dosage and Reactions

Drug	Dosage	Major Side Effects
Cyclophosphamide	100 to 150 mg/day in adults	- Haemorrhagic cystitis - Bone marrow suppression - Secondary malignancies
Azathioprine	2 mg/kg of body weight	- Bone marrow suppression - Secondary infection - Gastrointestinal upsets - Hepatotoxicity
Methotrexate	7.5 to 25 mg/ week	- Hepatotoxicity - Bone marrow suppression - Secondary infection - Diarrhoea
Cyclosporin A	5mg /kg per day of body weight	- Nephrotoxicity (75% cases) - Hypertension (25% casaes) - Gastrointestinal upset
Chlorambucil	2mg/day orally	- Hepatotoxicity - Bone marrow suppression - Gonadal dysfunction - Secondary malignancies

COMMON ETIOLOGIES OF POSTERIOR UVEITIS AND THEIR SPECIFIC MANAGEMENT

Common Etiologies of Posterior Uveitis



Idiopathic

Serpiginous choriodopathy

Senile Vitritis

APMPPE

MEWDS

Post Surgical

Bird shot retino choroidopathy

POHS

Frosted branch angitis

Idiopathic Uveal Effusion

Syndrome

Posterior scleritis

Toxoplasmosis

Toxocariasis

Tuberculosis

CMV retinitis

AIDS Related retinopathy

Collagen vascular disease

Behcet's disease

Vogt Koyangi Harada Syndrome

Syphilis

Sarcoidosis

Cysticercosis

Acute retinal Necrosis

Sympathetic Ophthalmia

Intraocular lymphoma

Pneumocystis Choroidopathy

COMMON INFECTIOUS ETIOLOGIES OF POSTERIOR UVEITIS

A) PARASITIC

(1) TOXOPLASMOSIS

Is the most common cause of infections retinochoroiditis in humans. It is caused by toxoplasmosis Gondii, an obligate intracellular protozoan parasite. Cat is the only definitive host. Human is the intermediate host. Toxoplasma Gondii exists in 3 forms.

i) Oocyst: Soil form (10 -12 μm)

ii) Tachyzoite : Active infections form (4 -8 μm)

iii) Tissue Cyst/Bradyzoite : Latent form (10 -12 μm)

Mode of Transmission to humans

1) Ingestion of Oocysts, which are shed in cat faeces and deposited in sand and soil around homes.
2) Ingestion of toxoplasma bradyzoites, the encysted form of parasite in undercooked meat (pork, beef, mutton & chicken)
3) Blood transfusion / organ transplantation
4) Direct innoculation of the tachyzoites, the proliferative form by accidental skin penetration with infected needles.
5) Transplacental transmission of tachyzoites
6) Ingestion of tachyzoites contaminated milk.

The diagnosis of Ocular toxoplasmosis is made by the following:

i) Observation of characteristics fundus lesion

ii) Detection of the presence of antitoxoplasma antibodies in the patient's serum

iii) Reasonable exclusion of other infectious diseases that might cause necrotizing lesions of the fundus principally syphilis, CMV, Fungus.

Clinical Features

Typical Manifestations

1) Focus of retinitis surrounded by fuzzy retinal Edema.

2) Pigmented Atrophic Retinochoroiditis scar adjacent to lesion or elsewhere.

3) Vitreous cells and exudates

4) Hyperemia of optic nerve head

5) Cells & flare in Anterior chamber

6) Patients with recurrent diseases - posterior synechiae, secondary cataract & Glaucoma.

Atypical manifestations

i) Juxtrapapillary Retinitis

ii) Retrobulbar neuritis

iii) Rhegmatogenous Retinal Detachment

iv) Pars Planitis

v) Outer Retinitis

vi) Serous macular detachment

- Although ocular toxoplasmosis has been considered to be a manifestation of congenital infection in most cases, reports of post -nately acquired ocular toxoplasmosis are increasing which show frequence recurrences.

Investigations

1) ELISA (Serum & Aqueous) - Antitoxoplasmosis IgG & IgM - Toxoplasma dye test of sabin feldman, the hemaggluttination lest, indirect immunofluorescent antibody test all provide approximately same information, however ELISA may offer more sensitivity & specificity. Any titer of serum antibodies is significant if the patient has a fundus lesion that is compatible with ocular toxoplasmosis. Titers higher in aqueous humor that in serum are more significant.

2) PCR of Aqueous aspirate

3) CT/MRI Brain in cases of Toxoplasmic encephalitis especially in immunosuppressed patients.

Treatment

The decision to treat generally would be based on the following criteria:-

i) A lesion within the temporal arcade

ii) A lesion abutting the optic nerve or threatening a large retinal vessel

iii) A lesion that has induced a large degree of haemorrhage

iv) A lesion that has induced enough of vitreal inflammatory response so that vision has dropped below 20/40 in a previously 20/20 eye or at least has sustained a two line drop from the visual acuity before the acute infection

Drugs

1st choice: Sulphadiazine + pyrimethamine + Folinic Acid

		Loading dose	Following dose	Duration
1)	Sulphadiazine	4 gm	1 gm daily (in 4 divided dose)	6 Weeks
2)	Pyrimethamine	150 mg	25 mg daily	6 weeks
3)	Folinic Acid	5 mg	5 mg daily	6 weeks

S/E : Sulpha Compounds: Skin rash, Crystalluria, Kidney Stones, Stevens Johnson Syndrome.

2st choice: Cindamycin + Pyrimethamine + Folinic Acid

		Loading dose	Following dose	Duration
1)	Clindamycin	600 mg	300 mg (in 3 divided dose)	6 Weeks
2)	Pyrimethamine	150 mg	25 mg (daily)	6 weeks
3)	Folinic Acid	5 mg	5 mg	6 weeks

S/E : Clindamycin: Pseudomembranous Colitis

Role of Cortiosteroids: They should be judiciously added to the regimen if the lesion is in the posterior pole or threatening the optic nerve head. Generally 20-40 mg/day in adult patient beginning 12-24 hrs after initiation of the specific antimicrobial therapy and try to taper in such a way that it is stopped before antitoxoplasma therapy is discontinued.

❖ Periocular Corticosteroids are not to be used.

(2) TOXOCARIASIS

Is the zoonotic disease caused by infestation of humans by the second stage larva of the dog nematode - toxocara canis or the cat nematode - Toxocara catis. Human beings are infected through ingestion of ova from contaminated food or by close contact with puppies.

Histopathology of lesion in Humans: Show granuloma formation around the larva & eosinophilic infiltrate.

Clinically human manifestation may take one of 2 forms

a) Visceral larva Migrans

b) Ocular Larva Migrans

Visceral Larva Migrans (Systemic Clinical Features): is seen in young children around 2 years of age with history of PICA. Symptoms include fever, nausea, coughing, wheezing, weight loss, hepatomegaly and pruritic eruptions over the body.

Ocular Larva Migrans (Ocular Features): May take 3 forms.

i. Peripheral Granuloma

Presentation: is usually during adolescence or adult life with visual impairment from distortion of the macula or retinal detachment. In an uncomplicated case lesion may remain undetected throughout life.

Signs: A white hemispherical granuloma may be seen at or anterior to the equator in any quadrant of the fundus. Vitreous bands frequently extend from the lesion to the posterior fundus. On contraction they may give rise to "dragging" of the disc.

Complications: Macular hetrotropia, tractional retinal detachment

ii) Posterior Pole Granuloma

Presentation: is between 6-14 yrs of age with unilateral visual impairment

Signs: Absence of uveitis. A round, yellow-white, solid granuloma between 1-2 discs in diameter centred in the juxtrapapillary or subfoveal location.

Complication: Retinal stress lines, vascular distortion, hard exudates surrounding lesion, subretinal hemorrhage and retinal detachment.

iii. Chronic Endophthalmitis

Presentation: is between 2-9 years of age with Leukocoria, Stratismus or unilateral visual loss.

Signs: Anterior uveitis and vitritis. The peripheral retina and parsplana may be covered by dense grayish white exudate similar to snow banking in pars planitis.

Complication: Hypotony, Cataract & tractional retinal detachment.

Differential Diagnosis

1) Retinoblastoma
2) Coat's disease
3) Persistent Hyperplastic Primary vitreous
4) Retinopathy of Prematurity, Familial Exudative Vitreoretinopathy, Peripheral trauma with peripheral traction.

Investigation

1. ELISA titer of Anti toxoplamosis Antibodies in serum, Aqueous & vitreous.
2. Cytological analysis of Aqueous and vitreous samples for Eosinophils.
3. USG: Highly reflective peripheral mass and vitreous bands.
4. UBM: Pseudocyst at Vitreous base.

TREATMENT

For peripheral Lesion - no treatment required.

For Posterior Pole Lesion:

Dinning and Colleague: 3 Step Approach is recommended which is

Local | Periocular Steriods | Systemic Steroids
+
Antihelminthic Therapy [Thiabendazole adults 800 mg 1 BD x 2 Week]
+
Combine Surgery if appropriate

3. CYSTICERIOSIS

Is caused by cysticercosis cellulosae, the larvae form of pork tapeworm, taenia solium. Humans get infected by drinking contaminated water or eating food-containing eggs of taenia soluim.

Clinical Features: It may affect any part of the eye from orbit to visual cortex but involvement of vitreous cavity and sub retinal space are common sites. Cyst appears as a translucent mass with a dense white spot at one region with a characteristic undulatory movement, which is absent in dead larva.

Rx: Surgical removal of cyst through parsplana route following vitrectomy is the treatment of choice.

B. BACTERIAL

1. TUBERCULOSIS

Intraocular involvement by Mycobacterium tuberculi remains presumptive one because these bacilli are only rarely isolated from clinical specimen. It is a relatively rare cause of posterior uveitis, although recently increasing due to AIDS epidemic. The diagnosis of intraocular tuberculosis is made if patient fulfils the criteria A with B/C.

A) Clinical suspicion of disease where any 2 of the following features are present:

i) Granulomatous anterior uveitis

ii) Active periphlebitis

iii) Neurorentinitis

iv) Retinochoroiditis

v) Subretinal Granuloma/Abscess

B) Corroborative evidence of the disease (any of the 2)

i) Mantoux ≥20mm / Necrosis

ii) Positive X-ray chest

iii) Aqueous /Vitreous tap positive for mycobacterium T.B. by PCR.

iv) Sputum positive for AFB on smear/culture/both

v) Histological evidence of Tuberculosis from cervical/parahilar lymph node

C) Response to antituberculous therapy (INH + Rifampicin + Pyrazinamide + Ethambutol).

Posterior Segment Manifestations

i. **Disseminated Choroiditis**: discrete, yellow, white/gray choroid tubercles, 0.5-3 mm in diameter associated with disc Edema and retinal Hemmorhage.

ii) **Focal Choroiditis**: present as single choroid tubercle about 2-3 DD in size with overlying serous Retinal detachment.

Treatment: ATT+ low dose steroids

2) SYPHILIS

Involvement of eye may occur by transmission of etiological agent, Treponema pallidum transplacentally (congenital syphilis) or venereally (adult syphilis). Uveal involvement is considered rare and usually occurs in the secondary stage of syphilis.

Clinical Features : Neuroretinitis or choroiditis (unifocal/multifocal) with varying grade of vitreous inflammation.

Treatment

The lesions may resolve spontaneously or by specific treatment using penicillin leaving behind hyperpigmentation and mimicing retinitis pigmentosa.

C. VIRAL

1) HERPES SIMPLEX & HERPES ZOSTER

Intraocular inflammation may manifest as either acute retinal necrosis or necrotizing herpetic retinopathy.

Acute Retinal Necrosis: is a fulminant, necrotizing viral infection of the retina. Urayama first described it in 1971. ARN occurs in healthy individuals of either age/sex. It may be bilateral in 33% of patients.

1) A designation of acute retinal necrosis should be made solely on clinical appearance and cause of infection. Clinical characteristic that must be seen include:

a) One or more focus of retinal necrosis with discrete borders located in the peripheral retina (primarily involving the area adjacent to or outside of the major temporal vascular arcades)

b) Rapid progression of disease (advancement of lesion borders or development of new foci of necrosis) if antiviral therapy has not been given.

c) Circumferential spread of disease.

d) Evidence of occlusive vasculopathy with arteriolar involvement

e) A prominent inflammatory reaction in the vitreous and anterior chamber.

2) Characteristic that support diagnosis include

a) Optic neuropathy/Atrophy

b) Scleritis

c) Pain

Complications: Rhegmatogenous Retinal Detachment (50- 75%)

Optic Atrophy

Investigations: ELISA (HSV, HZV, CMV) of Aqueous & Vitreous fluid

PCR for (HSV, HZV, CMV)

Treatment: Intravenous Acyclovir 150 mg/m^2/day in 3 divided doses X 10-14 days followed by oral Acyclovir 500 mg P.O. Prophylactic laser photocoagulation may prevent retinal detachment.

2) CMV RETINITIS

CMV is one of the Herpes virus and typically acquired during childhood. After primary infection virus becomes latent and resides in various tissues including leukocytes, salivary and lacrimal glands, periodic virus shedding occurs in blood, urine, respiratory tract. Clinical infection with CMV is a late manifestation of HIV infection and CMV retinopathy is seen virtually exclusively in patients with a CD4 T cell count of fewer than 100 cells/mm^3. Upto 40% of patients with CD4 T cells count lesser than 50 cells/mm^3 will develop CMV Retinitis.

C/F: Lesions consist of areas of creamy, yellowish white, full thickness retinal opacification with a variable amount of retinal hemorrhage . CMV lesions typically are large and often multiple and tend to follow the vascular supply of

the retina. The retinal vessels are abnormal in involved areas and show varying degrees of narrowing, occlusion and sheathing.Untreated there is always relentless slow progression of the disease until the retina is destroyed and vision is lost. Risk of Retinal Detachment has been estimated to be up to 50%

Pathology: Full thickness retinal necrosis with loss of all retinal architecture so that healthy retina is replaced by a glial membrane which is applied to RPE.

Diagnosis: Serology being of limited value due to prevalence of seropositively in large segment of population and also because of immunosuppression.

Treatment

1st Choice: Ganciclovir

2nd Choice: Foscarnet.

Ganciclovir I.V

- Treatment dose 5mg / kg IV BD x 14 -21 days
  Maintenance dose 6mg / kg OD x 5 days / week
- Administer by slow IV (over 1 hour in 100ml of 0.9% N saline)
- Monitor - complete Hemogram, LFT, Renal, and Electrolytes, Fundus examined during treatment.

Intravitreal therapy

6 injections over 2-3 weeks

Gancicolvir - 100 micro g - 200 micro g / 0.1ml

Foscarnet - 20 micro g / 0.1ml.

Intravitreal devices

- GIOD / Vitarest / Chiron Inc.
- Are the longest acting local form of therapy
- Dimensions of GIOD = Length 5-6mm
  Width 4mm
  Height 3.5mm
- Composition - 4.5mg of Gancicolvir coated on all sides except one by ethylene vinyl acetate.
- Duration of delivery = 5.8 months
- Inserted via parsplana with pellet facing the lens.
- Newer Agents - Cidofovir, Lobucavir, An antisense oligonucleotide (1515-2922), Anti CMV monoclonal Antibody MSL - 109.

3) HIV Associated Retinopathy: Posterior uveitis is most commonly infective in origin and is usually caused by CMV infection. Other causes include: -

i) **Toxoplasmic retinochoroiditis**: - is common in advanced HIV infection and usually is a newly acquired infection. Approximately 50% of HIV patients have coexistent CNS disease and should undergo neuroimaging. Toxoplasmic retinitis may appear quite atypical in HIV infection.

ii) **Mycobacterial choroiditis**: TB associated HIV is common in developing countries. T.B. uveitis is rare and usually characteristic multifocal choroiditis is seen.

iii) **Pneumocystis choroidopathy**: Single / multiple circumscribed yellow sub retinal lesions upto 2DD, which may slowly enlarge is seen.

D. FUNGAL

1. PRESUMED OCULAR HISTOPLASMOSIS SYNDROME

Is cause by fungus, histoplasma capsulatum that is endemic in certain regions of world like Missippi valley. Distinct feature is atrophic 'histo' spots; peripapillary atrophy, linear choroid atrophy and choroidal neovascularisation. Earliest symptom is metamorphopsia

Treatment:- FFA assisted Laser photocoagulation of CNVM.

2. CANDIDIASIS

It is a normal commensal which spreads hematogenously when immune system is compromised. Clinically lesions are multifocal, discrete, yellow white in early stages, they appears cottonball or string of pearls in vitreous.

Rx: Early recognition and antifungal drugs like flucytosine with ketoconazole.

COMMON NON INFECTIONS ETIOLOGIES OF POSTERIOR UVEITIS

A) Serpiginous choroidopathy - (Geogrophic Helicoid Peripapillary Choroidopathy)

This disorder gets its name from the 'snake' like pattern of spreading inflammation involving the choriocapillaries and retina. The disease affects both sexes between the ages of 40 and 60 years. Though involvement is bilateral the lesions are always asymmetrical. The exact etiology of disease is

unknown but recently association with tuberculosis & Herpes infection have been reported.

Clinical features: Symptoms - Blurred version, metamorphopsia, central and paracentral scotomas.

Signs:- Gray yellow discoid lesions deep to the retina involving RPE and choriocapillaries at the juxtra papillary, peripapillary region which progresses centrifugally in an irregular serpentine fashion with overlying edematous retina and vitreous haze. The underlying large choroidal vessels become prominently visible and there may be mild degree of pigmentary clumping also. Recurrences occur as creamy infiltration at the edges of previous scas. The disease commonly involves the macula "Macular GHPC" and has poor prognosis.

In chronic and recurrent cases - CNVM, Serous retinal detachment and areas of chorioretinal atrophy with subretinal fibrosis is seen.

INVESTIGATION

FFA : - **Active Stage**: Early Hypoflourescence with late Hyperflourescence.

Inactive stage: Mottled Hyperflourescence with late staining of scar.

ICGA: Active lesions Early Hyperflourescence with late staining.

Visual field: Absolute / Relative scotoma.

Treatment:

- The beneficial effect of medical treatment is controversial.

- However steroid and immunosuppressive is usually recommended.
- CNVM develop in 20% cases, which require laser photocoagulation.

B. SARCOIDOSIS

Is a multisystem disease that involves lung function primarily. Etiology is unknown. Pathologically the characteristic lesion is noncaseating granuloma. It usually presents in the 3rd decade (acute presentation or Heerfordt's disease) or insidiously in 5th decade (Lofgren's syndrome), it is also described in children more frequently.

Systemic Features are

- Pulmonary lymphadenopathy
- Erythema nodosum
- Hepatomegaly / Spleenomegaly
- Parotid enlargement
- Cardiomyopathy
- Arthopathy

Ocular Features are

- Acute / chronic nongranulomatous uveitis
- Vitreous snow balls
- Vitreous snow balls
- Retinal periphlebitis (Candle-wax dripping)
- Retinal, Choroidal Granulomas
- Preretinal (Lander's sign), Parapapillary & Optic Nerve Granulomas
- Papillidema
- Peripheral retinal neovascularisation

Investigation: Two most valuable tests are S.ACE and Chest X-Ray whenever this disease is suspected. Hypercalciuria is not an infrequent finding. Kveim antigen skin testing is positive in 85-90% of cases.

Treatment: Steroids are the mainstay of treatment; prolonged steroid therapy is however often poorly tolerated necessitating steroid sparing options such as low dose methotrexate.

C. Vogt-Koyanagi-Harada (VKH) Syndrome

Also known as uveomeningeal syndrome, is a multisystem disorder of unknown, possibly immune etiology, which occurs usually in patients between the third and fifth decade. It occurs most commonly amongst the Asians, particularly Japanese and has a HLA predisposition (HLA-DR4 & HLA DW15).

The disease normally progresses through a) uveitic b) convalescent c) chronic recurrent phases.

Ocular inflammation generally preceeds the integumentary changes but may also occur concurrently.

VKH Systemic Features

1. Cutaneous Alopecia/perilimbal vitiligo (Sugiura sign)
2. Neurological: meningeal irritation/cranial nerve palsies / convulsions
3. Auditory: (temporary 30%) - vertigo/tinnitis/deafness.
4. CSF pleocytosis.

VKH : Ocular features

1. Anterior uveitis - B/L granulomatous

2. Posterior uveitis - occurs in Harada's disease and proceeds as follows:-

i) Optic disc edema and multifocal detachments of the sensory retina with small folds radiating from the macular area.

ii) Coalescence of multifocal detachment, resulting in exudative RD

iv) Numerous residual small, mottled, atrophic scars known as `sunset glow' fundus develops about 4 weeks after uveitis.

FFA: is an important diagnostic tool; shows early pin point hyperfluorescent spots at the level of RPE which gradually enlarge as dye pools in sub retinal space

Treatment: Aimed at shortening duration of disease and preventing chronicity, and its complications. Early and aggressive use of systemic steroids followed by slow tapering over 3-6 months. Steroid resistant patients may require cyclosporin, azathioprine or chlorambucil.

D) BEHCET'S DISEASE

- is a systemic obliterative vasculitis of unknown cause, most commonly, seen in Mediterranean countries , middle east and far east eg. Japan.

- The disease affects young adults between 20-40 years of age more commonly men than women. It has been strongly associated with HLA B51.

International diagnostic criteria - Oral + any 2 of remaining 4

1. Oral: Minor/major apthae ulcers; recurrent atleast 3 times / 1Year.

2. Genital: recurrent genital apthae/scarring.
3. Eye: Anterior/Posterior uveitis; retinal vasculitis.
4. Skin: Erythema nodosum like lesions.
5. Pathergy: Positive pathergy test read by physician after 24-48 hours.

Ocular features

Anterior uveitis: Severe iridocyclitis with recurrent hypopyon.

Posterior uveitis: Acute Stage - vitritis, retinal vasculitis involving both arteries and veins, retinal hemorrhages, exudates, focal retinal infiltrates, papillits.

Chronic stage: Retinal ischemia giving rise to NVD and NVE, Neovascular glauoma, optic atrophy.

Treatment

1. Cytotoxic agents (Chlorambucil, Azathioprine, cyclosporine and cyclophosphamide)
2. Cortiosteroids

E) Acute Posterior Multifocal placoid pigment epitheliopathy (APMPPE)

Primary affection of retinal pigment epithelium of unknown cause, affects both sexes in 2-3rd decade with B/L involvement in most cases and is often preceded by flu like illness. The inflammation is confined largely to the

posterior pole and always within the equator. The lesions are initially multifocal but become confluent later.

IFA : Hypofluorescence in early stage and staining in later stages

Treatment: Natural course with patients regaining good vision.

F) Masquerade Syndromes

Group of disorders that occur with intraocular inflammation and often are misdiagnosed as chronic idiopathic uveitis. Because many of masquerade syndromes are malignant processes, early diagnosis and prompt treatment are crucial.

Eg. Malignant disorders: Intraocular lymphoma, leukemia, metastasis to eye uveal melanoma, retinoblastoma, xanthogranuloma

Non-malignant disorders: IOFB, retinal detatchment, myopic degeneration.

AIM OF THE STUDY

To evaluate the various etiologies of posterior uveitis and evaluate the effectiveness of treatment.

Introduction

v) Posterior uveitis is a diagnostic challenge "not only to general ophthalmologist but also to a uvea specialist" due to varied etiologies with their atypical manifestations and lack of specific diagnostic tests.

vi) We tried to find the various prevailing etiologies of this disease in our set up and to estimate the effectiveness of treatment by conducting a clinical study.

MATERIALS AND METHODS

The study design was a prospective case study of 70 patients who presented to Uvea clinic at Regional Institute Of Ophthalmology; G.O.H. during October 2004 - August 2005, for a period of 10 months.

Inclusion Criteria

vii) All patients of posterior uveitis who were first diagnosed in our clinic and not treated elsewhere.

Exclusion Criteria

viii) Post traumatic and post surgical uveitis cases.

ix) Anterior, intermediate and panuveitis cases.

x) Patients partially treated else where.

xi) Patients where follow up was less than 1 month.

xii) Patients with infective endophthalmitis, Eale's disease and lens induced uveitis.

All these patients were promptly questioned for present complaints, a detailed history is taken regarding the duration, onset, severity of attacks and previous such attacks.

Detailed systemic examination was done and if any abnormality was noted, concerned specialist opinion was sought and involved in proper management of case.

Thereafter visual acuity was recorded by Snellen eye chart. A detailed Slit lamp biomicroscopy with +90D/+78D/Hruby lens was carried out in most of our patients. Vitreous haze and cells were graded by retro illumination technique as described by kimura and colleagues.

Indirect ophthalmoscopy with scleral depression was done to rule out peripheral retinal involvement in most of our cases. The results were well documented by appropriate fundus drawings.

So on the basis of history and examination, the following naming - meshing system described by Nussenblatt et.al. was adopted.

1. Is the disease acute/chronic
2. Is the inflammation granulomatous/nongranulomatous
3. Is the disease unilateral/bilateral
4. What are the demographics of the patient
5. What are the associated symptoms and signs patient have

And after sorting out the list of probable causes in each group the differential diagnosis is generated for the each case. Based on this differential diagnosis the relevant investigation was ordered to confirm/refute the clinical suspicion. Other departments like retina clinic opinion were also sought to generate more clinical acumen regarding the disease.

We adopted a step up approach for various investigations ordered to necessitate our diagnosis. This approach was mainly self tailored according to the diagnostic value of the test, sensitivity, specificity of the test, its cost effectiveness, its availability and whether the test will make any difference to the treatment of patient

as described by Nozik et.al. Our investigation approach for various common diseases suspected in our study group is shown below.

	Suspected Disease	1st Choice Test		2nd Choice Test		3rd Choice test (if required)
1.	Toxoplasmosis	Indirect fluorescent antibody titer	→	Elisa antibody titer	→	PCR of vitreous sample
2.	Toxocariasis	Indirect fluorescent antibody titer	→	Elisa antibody titer, B-Scan	→	PCR, Eosinophil of Vitreous/ Acqeous Sample
3.	Serpiginous choroidopathy	FFA	→	ICGA		
4.	CMV retivitis	Elisa HIV CD4/CD8 count	→	FFA urine and serum culture (in paediatric)		
5.	Tuberculosis	Montoux, chest x-ray, ESR, Sputum, AFB	→	PCR T.B. of Serum	→	PCR T.B. of Vitreous
6.	Collagen Vascular Disease	Rf., ANA, ANCA	→	Serum Anti DNA Abs. Anti Phospholipid Antibodies.		
7.	Vogt Koyanagi Harada	FFA	→	HLA typing	→	lumbar puncture in acute stages for pleocytosis
8.	Acute Retinal necrosis	FFA				
9.	Sarcoidosis	CXR, serum ACE Serum/A/G ratio	→	HRCT Chest scan conjunctival biopsy		
10.	APMPPE	FFA	→	ICG		

Investigation Protocol

Patients were treated as per the guidelines (discussed before) given for each specific disease though cost constraints/drug availability did prevent us from adopting the first line of choice of treatment in some cases.

All our patients were advised to strictly adhere to the treatment protocol and follow up visits. Non-compliance to drugs either due to patient socioeconomic factors or side effects were sought in each follow up visits.

At each follow up visit, the patient visual acuity was assessed, asked for symptoms complex, detailed ocular examination was done, and following which patients was advised to adjust the dosage of drugs. During our follow up we tried to grade the category of our treatment response in categories like;

Status quo / worsening / improving / recurrence / steroid-dependency / immunosuppressant requirement / surgical procedure required.

Our approach to various diseases were: -

1. Idiopathic

This large group of cases where etiology was unknown was usually treated with periocular steroids and systemic steroids as we have ruled out most of the infective etiologies. This group of patients was more closely and regularly followed up as we were not aware of the cause in these cases.

2. Infective & Non Infective Etiologies and our choice of treatment

We tried to strictly follow the duration of treatment for the specific infective etiologies though our tailored choice was as follows:-

	Disease	1st Choice Drug		2nd Choice Drug
1.	Toxoplasmosis	T.Cotriamazole (DS)	→	T.Azithromycin
2.	Toxocariasis	Steroids	→	Thiabendazole
3.	Serpiginous choroidopathy	Corticosteroids (systemic)	→	Immuno suppressant Azathiopnine
4.	CMV retinitis	HAART with reference to other institute for IV ganciclovir/ implants.		
5.	Tuberculosis	ATT with low dose steroids		
6.	Collagen Vasc. Disease	Corticosteroids	→	I.V. Cyclophosphamide pulse
7.	VKH	High dose of systemic corticosteroids and I.V. methyl prednisaline	→	Immunosuppressants
8.	Acute Retinal necrosis	I.V. Acyclovir followed by oral Acyclovir		
9.	Sarcoidosis	Corticosteroids with referral to internal medicine department for complete treatment		
10.	APMPPE	Follow up of patient alone		

Treatment Protocol

After this analysis of our observations were made using various statistical tools like mean, average, standard deviation and probability charting, t - test and null hypothesis were used whenever required.

ANALYSIS AND OBSERVATION

1. Number of patients enrolled in our study = 102
Patients lost during follow up period = 32
Final number of patients available for analysis= 70
Range of Follow up period = 1-11 months
Mean average of follow up period = 2.3 months/ individual

2. Age Incidence

Year Group	No. of Patients	Percentage
0-10 Years	4	6%
10-20 Years	5	7%
20-30 Years	8	11%
30-40 Years	20	30%
40-50 Years	15	21%
50-60 Years	8	11%
> 60 Years	10	14%

Mean Age Incidence was 37.8 years ± 10.1 years (2S.D) in our study. The higher incidence of uveitis in 3rd-4th decade was also seen in other major studies. Also we noticed toxocariasis cases commoner in younger age group and Serpiginous choroidopathy cases commoner in elderly patients.

3. Sex Incidence

	No. of Patients	Percentage
Male	38	54%
Female	32	46%

Males out numbered females in our study. Mean age of onset in males was 36.7 years. Mean age of onset in females was 38.8 years. Males preponderance was noted in previous other studies also

4. Laterality

	No. of Patients	Percentage
RE	19	27%
LE	17	24%
Both eyes	34	48%

Bilateral involvement was commoner than unilateral involvement and no eye has a predominant predilection.

5. Course of disease

	No. of Patients	Percentage
Acute	18	26%
Chronic	37	53%
Recurrent	15	21%

26% of our patients have acute course i.e. inflammatory response lasting < 3 months. 53% of our patients have chronic course of disease i.e. inflammatory response lasted for longer than 3 months. 21% have recurrent uveitis i.e. 3 or more episodes of intraocular inflammation.

6. Presenting Complaints

	No .of Patients	Percentage
Floaters	16	23%
Diminished vision	30	43%
Pain	5	7%
Photophobia	8	11%
Redness	5	7%
Watering	5	7%
White Eye Reflex	1	2%

Diminished vision (43%) and floaters (23%) were the commonest complaints in our patients. These being the most common symptoms reported in posterior uveitis in other major studies as well.

Prominent Medical History

	No.of Patients	Percentage
Diabetes	8	11%
Hypertension	8	11%
Tuberculosis	4	6%
AIDS	3	4.5%
Cancer	1	1.5%
Arthritis	4	6%
Collagen Vascular disease	2	3%

We found close association of CMV Retinitis patients with AIDS.

Prominent Medical Symptoms

	No.of Patients
Fever	10
Weightloss	4
Hair Loss	3
White skin patch	2
Rash/Intertrigo	6
Nodules	1
Skin sores	5
Photosensitivity	2
Painful Joint	4
Swollen joint	2
Low back pain	2
Stiff joint	1
Mouth ulcer	1
Dental caries	14
Dental gingivitis	8
Difficulty in breathing	3
Headache	2
Hoarseness	4
Ear discharge	2
Vaginal discharge	3
Vaginal itching	3

7. Dietary History

	No.of Patients	Percentage
Veg	28	40%
Non Veg	42	60%

8. Personal History

	No. of Patients
Owned pets	3
Close contact with dog/puppy/cat	8
Treated water usage	18
Untreated water usage	52
Unprotected sexual intercourse	4
Pregnancy	3
Drug Allergies	4

We found uncooked meat, untreated water usage and close contact with pets were associated with toxoplasmosis and toxocariasis cases.

9. Systemic Associates

	No.of Patients	Percentage
Skin	16	22%
Dental	22	31%
ENT	6	8.5%
Rheumatology	9	12%
Gynecology	7	10%
Internal medicine	7	10%

Dental foci were common association in patients with idiopathic posterior uveitis. Null hypothesis was applied and results were statistically significant ($p < 0.1$). Skin foci were also commonly associated was also statistically significant ($p < 0.05$).

10. Type of Choroiditis

Pattern	No.of Patients	Percentage
Focal	5	11%
Multifocal	31	67%
Diffuse	10	22%

67% our patients had multifocal choroiditis type of anatomical involvement. This was also seen in other major studies.

11. Etiological Diagnosis

	No.of Patients	Percentage
Idiopathic	30	42.8%
Infective	27	38%
Non Infective	13	18%

43% of our cases were idipathic ie. The intraocular inflammation could not be attributed to a specific ocular cause. The remaining 57% were due to infective or non-infective etiologies.

Clinical Diagnosis

	No.of Patients	%
Idiopathic	30	42.8%
Toxoplasmosis retinochoroidits	12	17.1%
Toxocariasis retinochoroidits	8	11.4%
Serpiginious choridopathy	8	11.4%
CMV retinitis	4	5.7%
Tuberculosis retinochoroiditis	2	2.8%
Collagen Vascular disease retinitis	2	2.8%
Vogt Koyanagi Harada syndrome	1	1.4%
Acute retinal necrosis	1	1.4%
Acute posterior multifocal placoid pigments Epitheliopathy	1	1.4%
Sarcoidosis	1	1.4%

Toxoplasmosis (42.8%), Toxocariasis (17.1%), Serpiginous choroidopathy (11.4%) & CMV retinitis (11.4%) accounted for major number of cases in our study. The comparison with other studies is drawn in discussion.

12. Immunofluorescent Antibody assay of TORCH Titers

Type of antibody	No.of patients with positive titers	%
1. IgG Toxoplasmosis IgM Toxoplasmosis	20 12	28% 17%
2. IgG Toxocariasis IgM Toxocariasis	6 6	8.5% 8.5%
3. IgG Rubella IgM Rubella	9 5	13% 7%
4. IgG Cytomegalovirus IgM Cytomegalovirus	24 13	34% 18%
5. IgG Herpes simplex Virus I IgM Herpes simplex virus II	5 5	7% 7%
6. IgG Herpes Simplex Virus II IgM Herpes Simplex virus II	6 5	8.5% 7%
7. IgG Treponema pallidum IgM Treponema pallidum	5 3	7% 4%

Significant number of clinical suspicious cases of toxoplasmosis showed IgM positive titers and high IgG titers. CMV positivity rates were high in our case series (34%) although not associated with disease in majority of cases.

13. FFA findings

Findings	No. of Patients	%
Papillitis	11	16%
Vasculitis	16	23%
CNVM	6	8.5%
Cystoid macular edema	16	23%
Active choroiditis	12	17%
Old Scar staining	22	32%

Staining of Scar tissue (32%) vasculitis (23%), Cystoid Macular Edema (17%) were commonest findings in FFA study.

14. Treatment Groups - Medical

Type of Treatment	No.of Patients	%
Systemic steroids	46	40%
Periocular steroids	24	21%
Topical steroids	20	17%
Immunosuppresants	7	6%
Specific therapy against infections	18	16%

Majority of our cases were started on combination of systemic and Periocular steriods (61%) only few were treated with immunosuppresants (6%)

15. Change in Vision % on Snellen after steroid use

Snellen chart	No.of Patients	%
Increase in > = 2 Lines	17	25%
No change	46	65%
Decrease > = 2 lines	7	10%

We found improvement in 25% of our cases and no worsening in 66% of patients on mean of 3 months of steroid usage.

16. Steroid Responsiveness

	No.of Patients	%
Steroid responders	36	65%
Steroid non responders	8	14.5%
Recurrence on steroids	5	9%
Steroid dependence	6	10%

17. Response to Specific Therapy

Response	Antitoxo plasmosis	Anti toxocariasis	Anti CMV	Anti viral	Anti tuberculosis
Improving	7	2	1	0	2
Worsening	2	1	1	1	1
Status quo	3	5	2	1	1

58% of toxoplasmosis patients, 50% of tuberculosis patients, 25% of toxocariasis and 25% of CMV Retinitis patients showed improvement to specific therapy against the infection.

18. No. of patients requiring immunosuppressants

	No. of Patients	%
Methotrexate	2	3%
Azathioprine	3	4%
Cyclophosphamide	2	3%

We used immunosuppressants in 7 of our patients - mostly for Serpiginous choroidopathy and steroid - non responders and recurrence on steroids group of patients.

19. Intraocular Surgery Required in

Type of Surgery	No. of Patients	%
Cataract	13	18%
Vitrectomy	6	8.5%
Filtering	6	8.5%

20. Final Visual Acuity in treatment group

Visual Acuity	> 6/9	%	6/12-6/36	%	<6/60	%
Before Treatment	17	24	21	30	12	17
After Treatment	25	35	17	24	10	14

24% of Patients with visual acuity >6/9, increased to 35% and 17% of patients with visual acuity <6/60 decrease to 14%. Both signified improvement in visual acuity after treatment.

DISCUSSION

Differential Diagnosis of Posterior Uveitis is extensive with the pattern of uveitis keep changing with time and with the emergence of new uveitic entities. Various genetic, ethnic, demographic and environmental factors also influence the patterns. Our study results were compared with 4 recent major studies to compare any such change in patterns

1. Biswas et al. "Pattern of uveitis in a referred uveitis clinic in South India" International Ophthalmology Journal 1996-1997; 20: 223-28.
3. Rodriguez et.al. "Pattern of uveitis in a tertiary Eye care centre" Archives Ophthalmology 1996; 114" 593-599.
3. Biswas et al. "Changing Patterns of uveitis in a referral uveitic clinic in India" AIOS proceedings 2000.
4. Ramandeep Singh et.al. "Patterns of uveitis in a referral Eye clinic in North India" IJO June 2004; 52; 121-125.

POSTERIOR UVEITIS ETIOLOGIES

Disease Etiology	Our Study	Biwas et.al. 1996	Rodriguez et al. 1996	Biswas et.al. 2000	Ramandeep et.al. 2004
Idiopathic	**42.8%**	40.9%	13.3%	5.25%	24.7%
Toxoplasmosis	17.1%	**27.8%**	24.6%	9.83%	8.0%
Serpiginous	11.4%	18.8%	1.6%	**35.26%**	25.1%
Toxocariasis	**11.4%**	5.8%	2.5%	4.05%	2.5%
CMV Retinitis	5.7%	0.55%	**11.6%**	6.25%	1.21%
Tuberculosis Retinochoroiditis	2.8%	2.16%	0.6%	1.32%	**8.9%**
Collagen Vascular Disease Retinitis	2.8%	5.0%	**7.9%**	5.0%	3.0%
Acute Retinal Necrosis	1.4%	0.82%	**5.5%**	1.73%	3.2%
APMPPE	1.4%	1.37%	2.0%	**2.31%**	1.6%
VKH	1.4%	8.0%	5.0%	6.25%	**16%**
Sarcoidosis	1.4%	5.0%	**7.5%**	4.25%	0.8%

The various inferences drawn are

1) Idiopathic cases (42.8%) accounted for the largest group in our series of patients. This was comparable to initial study by Biswas et.al. 1996 - (40.9%). But it was significantly higher comparing to studies by Ramandeep et al. 2004. The reason accounting would be due to non-availability of certain expensive tests under our purview like PCR for T.B, chorioretinal biopsy etc.

2) Toxoplasmosis (17.1%) cases were the leading cause of Posterior uveitis in our group which tallied with other studies of Biswas et.al. 1996, Rodriguez et.al. 1996. However the percentage of cases were lower than that reported by Holland and Engstrom (30% - 50%). Notingly Ramandeep et al. 2004 in the recent study reported only 8.0% of posterior uveitis cases as toxoplamosis and Biswas et.al. 2004 reported only 9.85% and felt that reason for decrease in referral was that many of the cases were congenital and usually healed. Although we reported high incidence were of Toxoplosmosis which were active.

3) Serpiginous choroidopathy being the 2nd major cause (114%) in our study confirms the high prevalence of this disease in Indian subcontinent as evidence by the previous Indian studies - Biswas et.al. 1996 (18.8%), Biswas et.al. 2000 (35.26%) and Ramandeep (25.1%) in comparison to Rodriguez study 1996 at Boston (1.6%). But incidence in our study was not as high as reported by Ramandeep et.al. and Biswas et al. Neither we found any significant correlation between tuberculosis and Serpiginous Choroiditis as reported by Ramandeep et al.

4) We reported significantly higher number of cases of toxocariasis in our study (11.4%) equaling the number of cases of Serpiginous choroiditis and much higher than previous studies reported in India. The reasons being largely unknown but majority of our cases were children and

significant history and PICA/association with pets were noted in these cases. This represent a changing trend in the current scenario of etiologies of posterior uveitis.

5) CMV Retinitis cases were also substantial (5.7%) comparable with the earlier studies of Rodriguez et al. 1996 (11.6%). All these cases were positive for HIV ELISA signifying the commonest retinal lesion in HIV patients being CMV retinitis. Also signifying the increasing incidence of HIV patients in Indian subcontinent.

6) Tuberculosis retinochoroiditis (2.8%) casaes were less reported in our study group comparing with Ramandeep et.al. (8.9%) the reasons being the use of PCR for mycobacterium tuberculi on vitreous sample by the author; so the hidden cases were detected. We acknowledge our inability to pick up these hidden cases. Prevalence of Tuberculosis retinochoroiditis could be higher as shown in the above study.

7) We reported only Systemic Lupus Erythromatosus as a cause in our collagen vascular disease retinitis (2.8%) group. This was significantly lower than reported by Rodriguez et.al. 1996 (7.9%).

8) Other cases like Acute retinal necrosis, Acute posterior multifocal placoid pigment Epitheliopathy, VKH Syndrome accounted for few other cases. These new disease entities are increasingly detected due to increased awareness among ophthalmologists.

Our Study also analysed the effectiveness of various specific treatment modalities in our patients with different etiologies, Results were comparable with previous studies like-

1) Effectiveness of treating ocular toxoplasmosis by a course of TMP-Sulphamethoxazole (TMP = 5 mg/Kg, sulphamethoxaxole 25 mg/Kg) for period of 1 month with concomitant use of systemic steroids. We reported dramatic healing in 7 out of 12 cases with decrease in sign &

symptoms. The results were comparable with Torre et.al. Randomized trial of TMP-Salphamethoxazole versus Pyri-sulphadiazine for therapy of toxoplasmosis, Antimicrobial agents chemotherapy 1995, 42: 1346-1349.

2) We reported marginal improvement in patient with pregnancy with macular choroiditis due to Toxoplasmosis on treatment with T.Spiramycin comparable with previous study by Wing S, Remington: Toxoplasmosis in pregnancy Clinical Infectious Disease 1994, 18: 853-62.

3) Treatment trial with immunosuppressants was beneficial in Serpiginous choroiditis cases, which showed significant response by preventing disease activity and macular involvement. This was comparable to Biswas et.al. - Immunosuppressants role in Serpiginous choroidopathy in the "changing patterns of uveitis in tertiary care centre".

4) Response to Thiabendazole therapy in our patients with active toxocariasis lesion when given concomitant with steroids was not very substantial. We need to do further treatment trials to come to any firm conclusion regarding its benefits.

5) Response to CMV Retinitis patients to IV.Ganciclovir and HAART Therapy and ATT for Tuberculous Retinochoroiditis was mixed. 50% patients in each group improved after therapy or remained status quo.

6) Both of our patients with SLE Retinitis went for consequetive optic Atrophy inspite of being treated with pulses of Cyclophosphamide and steroids. Patient with Acute Retinal Necrosis didn't show much improvement in final visual acuity even after IV acyclovir and oral acyclovir treatment.

7) Patients with VKH syndrome and sarcoidosis showed good response to systemic immunosuppressant therapy.

8) Finally we assessed the response of Idiopathic and non infectious posterior uveitis cases to systemic and periocular steroids and found 25% of case showed increase in ≥ 2 lines of visual acuty on Snellens chart on 3 months follow up with no worsening in 65% of cases. This was significant statistically ($p < 0.1$) and results were comparable with other major studies.

9) We found 10% steroid dependence rates with 15% of patients were steroid non-responders 9% of patients showed recurrence on steroids. In these groups addition of 2nd line immunosuppressants allowed reducing the dose of systemic prednisolone as well in controlling inflammation and reducing the number of relapses to a significant extend comparable with study on clinical outcome of chronic immunosuppression in non infectious uveitis by "Victor et.al. Clinical & Experimental ophthalmology 2005; 33:16-21.

10) Also the efficacy of posterior subtenon was similar to orbital floor injections in our study group.

SUMMARY

1) The most common age group is 31-40 years in our study with mean follow up period of 2.3 months / individual.

2) Male preponderance was noted with both eyes involvement commonly seen.

3) Most of patients had chronic course of disease.

4) Most common symptoms were floaters and diminished vision.

5) Significant association was seen in patients with untreated water usage, uncooked meat and closed contact with pets with diseases like Toxoplasmosis & Toxocariasis.

6) Dental & Skin foci of infection has a common association with Idiopathic posterior uveitis cases.

7) Anatomically multifocal choroiditis was the commonest pattern.

8) TORCH Immunofluorescent Antibody assay gives good corroborative evidence of disease based on clinical suspicion although the sero conversion is more significant than a single high reading.

9) CMV Seropositivity rates were high in our population and don't warrant any active treatment in the absence of lesion.

10) Toxoplasmosis, Toxocariasis, Serpiginous Choroidopathy and CMV Retinitis associated with HIV infection were the major etiological causes identified in our series of patients.

11) Response to specific therapy to toxoplasmosis was good.

12) Serpiginous Choriodopathy patients showed good response to immunosuppressants.

13) Response to steroids is noninfective idiopathic cases was substantial.

CONCLUSION

Posterior uveitis remains a diagnostic challenge to the ophthalmologist. By knowing the present changing trends and geographical patterns help him to err on the approach of "Common things are more common and to be considered in Diagnosis first". Also it helps him to focus on new emerging uveitic entities.

We were able to achieve a good discretion of some common causes of posterior uveitis like Toxoplasmosis, Toxocariasis and Serpiginous choroiditis and recommended the importance of detailed clinical history and clinical examination.

The recent drugs available against them were found to be really effective except toxocoriasis treatment.

The investigations have to be undertaken with clear objectives and not irrationally to avoid unnecessary expenditure for the patients. We found the effectiveness of TORCH titers in providing corroborative evidence of diseases in cases of posterior uveitis.

PROFORMA FOR POSTERIOR UVEITIS

Government Eye Hospital
Egmore, Chennai

M.R.No.
Uvea No.
Date

I. Name Occupation Age/Sex Address
Occupation Community

2. Present History

	RE	LE	Duration	Onset	Severity	Course
Pair				Acute/Insi	Mild/Mod/Sev.	Acute/Chronic/Rec.
Redness				Acute/Insi	Mild/Mod/Sev.	Acute/Chronic/Rec.
Photophobia				Acute/Insi	Mild/Mod/Sev.	Acute/Chronic/Rec.
Floaters				Acute/Insi	Mild/Mod/Sev.	Acute/Chronic/Rec.
Defective vision				Acute/Insi	Mild/Mod/Sev.	Acute/Chronic/Rec.

Any other specific complaints

H/O previous attack :- Treated/Not treated

II. General Medical History and review - fever/night sweats/weight loss

1. Systemic illness : Diabetes, Hypertension, tuberculosis, cancer, AIDS, Arthritis, collagen vascular disease, fever
2. Skin : Vitiligo, alopecia, poliosis, rash, nodules, sores, Sunburn Easily.
3. Joints : Painful or swollen joints, low back pain, stiff joints.
4. GIT : Painful mouth ulcers, stomach ulcers, bloody stools.
5. Dental : Caries, gingivitis, pain in teeth, tooth loss, recent surgery.
6. Pulmonary : Cough more than 3 months, hemoptysis, difficulty in breathing.
7. ENT : Frequent sneezing, sinus trouble, hoarseness, ear Discharge, tinnitis
8. GUT : Genital ulcers, penile discharge
9. Gynec : Vaginal discharge, itching

III. Past h/o: - D.M./HTN/T.B./Herpes/Shingles/Any sexually transmitted disease / Eye / General Surgeries.

IV. Family history : T.B./Arthritis/diabetes/cancer

V. Personal History

- Contact with dog/cat/puppies/sick animals
- h/o of pica (especially in children)
- Vegetarian - Raw Uncooked sausage
- Non-vegetarian — Uncooked meat, Pork/Beef/Steak
- Water - Untreated water/treated water
- H/o unprotected sexual exposure
- Pregnant/near future plan

VI. History of drug allergy - Esp. sulpha group, Penicillin

VII. Summary of History

- Acute/chronic
- Unilateral/bilateral
- Demographic details

Age <15 yrs - Toxocariasis
Age 15-45 yrs. - Toxoplasmosis, ARN, AIDS, VKH
Age > 45 yrs - Serpiginous, Birdshot

Sex female - JRA
Male- AS, Sympathetic

Any Striking detail

VIII. General Examination

Anemia/Lymphadenopathy

IX. Skin :
Dental :
ENT :
Rheumatology :
Gynecology :
CVS :
RS :
GIT :
CNS :

X. Ocular Examination

		RE	LE
i.	Vision		
ii.	Conjunctiva		
iii.	Cornea		
iv.	AC Flare Grade		
	Cells grade		
	Hypopyon		
v.	Iris		
vi.	Pupil		
vii.	Lens		
viii.	Vitreous		
	Flare Grade		
	Cells Grade		
	Debris		
	Strands		
	Hemorrhage		
	Miscellaneous		
ix.	Retina		
	Disc		
	Vessel		
	Macula		
	Posterior pole		
	Periphery		
	Miscellaneous		
x.	Choroid		
	Choroiditis	Location -	Location -
	Focal Granuloma	Number -	Number -
	Multifocal	Appearance -	Appearance -
	Diffuse/geographic		
	Serous retinal Detachment		
	Hard exudates		
	Old Scars		
	Pigmentation		
	CNVM		
	Miscellaneous		

		RE	**LE**
xi.	Fundus		
xii.	Laboratory test	Results	
1.	Blood Hemoglobin		
	Total Count		
	Differential count		
	ESR		
	CRP		
	CD4+/CD8+		
	Culture		
2.	Urine Routine		
	Culture		
3.	Serum ANA		
	ANCA		
	Rf		
	Anti DNA Abs.		
	ACE		
	Ca^{+}		
	A/G Ratio		
	Lysozyme		
	VDRL		
	TPHA		
4.	Immunofluroscent Antibody assay	IgM	IgG
	Toxoplasmosis		
	Toxocariasis		
	Rubella		
	CMV		
	Herpes Simplex Type I		
	Herpes Simplex Type II		
	Treponemal		
5.	Elisa HIV	Results	
	Western Blot HIV		

		RE	LE
6.	Radiological		
	Chest X-ray		
	Skill X-ray (lateral view)		
	CT/MRI Brain		
	HRCT Chest		
7.	Skin Test		
	Mantoux		
	Pathergy		
	Kveim		
	Anergy		
8.	HLA typing		
	HLA B-27		
	HLA B-5		
	HLA A-29		
	& MT3/HLA BW 22J		
9.	Fundus fluorescein angiography		
10.	Indocyanine green angiography		
11.	Ultrasonography		
12.	Skin/Gland/Hair Biopsy		
13.	Aqueous/Vitreous Sample		
	Cytology		
	Staining		
	Culture		
	PCR		
14.	Chorioretinal Biopsy		
15.	Specialists Opinion		
	Skin		
	Dental		
	ENT		
	Rheumatology		
	Gynecology		
	Paediatric		
	Chest & T.B.		
	Neurology		
	Internal medicine		
	Diabetology		
	Hypertensive Clinic		

		RE		LE	
xiii.	Clinical Diagnosis	Infective/noninfective/idiopathic		Infective/noninfective/idiopathic	
xiv.	Differential diagnosis	On basis of history /age / sex / demographic / lateralilty / onset / granulomatous / nong. Appearance/Tests			
xv.	Treatment				
	Medical				
	- Corticosteroid (Topical)				
	(Periocular)				
	(Systemic)				
	- Specific Therapy				
	- Immunosuppressants				
	- Any other medications				
	Surgery - Cataract /vit. / Glaucoma				
xvi.	Followup visits & Plan	**Date**	**Visual acuty and response**	**Date**	**Visual acuty and response**
	Status quo (•)				
	Worsening (↓)				
	Improving (↑)				
	Recurrence (*)				
	Steroid Dependency ( )				
	Surgery planned (x)				
	Addition of immuno suppressants (+)				
xvii	Final comments				

KEYS TO MASTER CHART

P = Pain
R = Redness
PH = Photophobia

F = Floaters

DV = Diminished Vision
DY = Days
MO = Months
YRS = Years
COUR: Course of Disease
AC = Acute
CHR = Chronic
REC = Recurrent
LAT = Laterally
OD = Right type
OS = Left eye

OU = Both Eyes

DM = Diabetes Mellitus

HTM = Hypertension
TB = Tuberculosis
GP = GIT Problem
RP = Respiratory Problem
JP = Joint Problem
DF = Dental Foci
EF = ENT Foci
SF = Skin Foci
GF = Gynec.foci
V = Vegetarian
NV = Non vegetarian

PR - Pregnant
UPS = Unprotected sexual intercourse
Sys/SpecEx-Systemic & specialty examination
CCC = Circumcomeal congestion
KP = Keratic Precipitates
FL = Flare in Anterior Chamber
CE = Cells in Anterior Chamber
HY = Hypopyon

VS = Vitreous Strands
VHAEM = Vitreous Hemorrhage
IPVD = Incomplete posterior vitreous detachment
CPVD = Complete posterior vitreous detachment
DE = Disc Edema
DH = Disc Hyperemia
OA = Optic Atrophy
VA = Vessel Attenuation
VO = Vessel Obliteration
VASC = Vasculitis
VASS = Vascular Sheathing
CME = Cystoid macular edema
MH = Macular Hole
MP = macular pigmentation
TRD = Tractional Retinal detachment
ERD =Exudative Retinal detachment
RRD = Rhegmatogenous retinal detachment
RE = Retinal edema
RH = Retinal hemorrhage
HEX = Hard Exudates
SEX = Soft Exudates
ERM = Epiretinal membrane
MCM = Multifocal chroidal mass
DCM = focal choroidal mass
MACC = Macular choroiditis
OLDC = Old Choroiditis Scar
POL = Punched out lesions
ACE = Angiotension converting enzyme
TREP = Treponema pallidium
Toxop = Toxoplasmosis
Toxoc = Toxocariasis canis

RUB = Rubella
CMV = Cytomegalo virus
HSVI = Herpes Simplex Virus I
HSVII = Herpes Simplex Virus II
CXR = Chest X-ray

PS = Posterior Synechia
PSC = Posterior subcapsular cataract
VH = Vitreous flare
VC = Vitreous cells
VD = Vitreous debris
CM = Cardiomegaly

MX = Montoux
EHP = Early hypofluorescence
LHY = Late Hyper fluorescence
LEAK = Leakage
CNVM = Choroidal neovascular membrane
DS = Disc Staining
LMS = Margins of Lesion Staining
TOXOPRC = Toxoplasmosis retinochoroditis
TOXOCRC = Toxocariasis retinochoroiditis
SERPC = Serpiginous choroidopathy
CMVR = CMV Retinitis
CVDRC = Collagen vascular disease
TUBRC = Tuberculosis retinochoroiditis
VKH = Vogt Koyanagi Harada Syndrome
ARN = Acute Retinal Necrosis
APMPPE = Acute Posterior Placoid Pigment Epitheliopathy
SARC = Saroidosis
ST = Topical steroids
SP = Periocular steroids
SS = Systemic steroids
I = Immuno suppressant
MTX = Methotrexate
AZT = Azathioprine
CP = Cyclophosphamide
ACY = Acyclovir
ATT = Anti Tuberculosis therapy
SPF = Sulpha + Pyri + FA
SEP = Septran
THIA = Thiabendazole

SXR = Skull X-ray
HRCT = High resolution CT Scan
LN = Lymph nodes
CAL = Calcification
SIN = Sinusitis
HAART \ HIV Anti retroviral therapy
SX = Surgery
CAT = Cataract Surgery
VIT = Vitrectomy
FIL = Filtering surgery
↓ = Worsening

↑ = Improving
• = Status Quo
* = Recurrence

= Steroid Dependence

+= Addition of immunosuppressants

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